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(54) Title: GENOME PARTITIONING

(57) **Abstract:** This invention relates to 'genome partitioning' and nucleic library construction, for example for sequence variation discovery and screening. The method employs a plurality of restriction enzymes in order to reliably reproduce a representative partition of the entirety of a sample nucleic acid based on the restriction ends of one or more 'layers' of the fragments present. In preferred embodiments there is provided a method for producing a nucleic acid library, which library contains a plurality of different nucleic acid fragments, the method comprising: (i) digesting the sample nucleic acid with a plurality of different restriction enzymes to generate a plurality of different layers of fragments, wherein each layer is a group of fragments having a unique combination of restriction ends, and wherein the combination of layers represents the entirety of the sample nucleic acid, (ii) optionally purifying said fragments, (iii) selecting a desired sub-set of layers according to the unique restriction ends of said layers, (iv) ligating said sub-set of layers into vectors adapted to receive it, (v) transforming host cells with the vectors (vi) culturing said host cells to provide said library containing said partition of the sample nucleic acid. The invention also provides systems, methods and functions for designing and optimising such libraries, and genotyping 'chips' based on the genome partitioning methods.

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